

SUGAR-CONTAINING AMPHIPHILIC OLIGOMERS

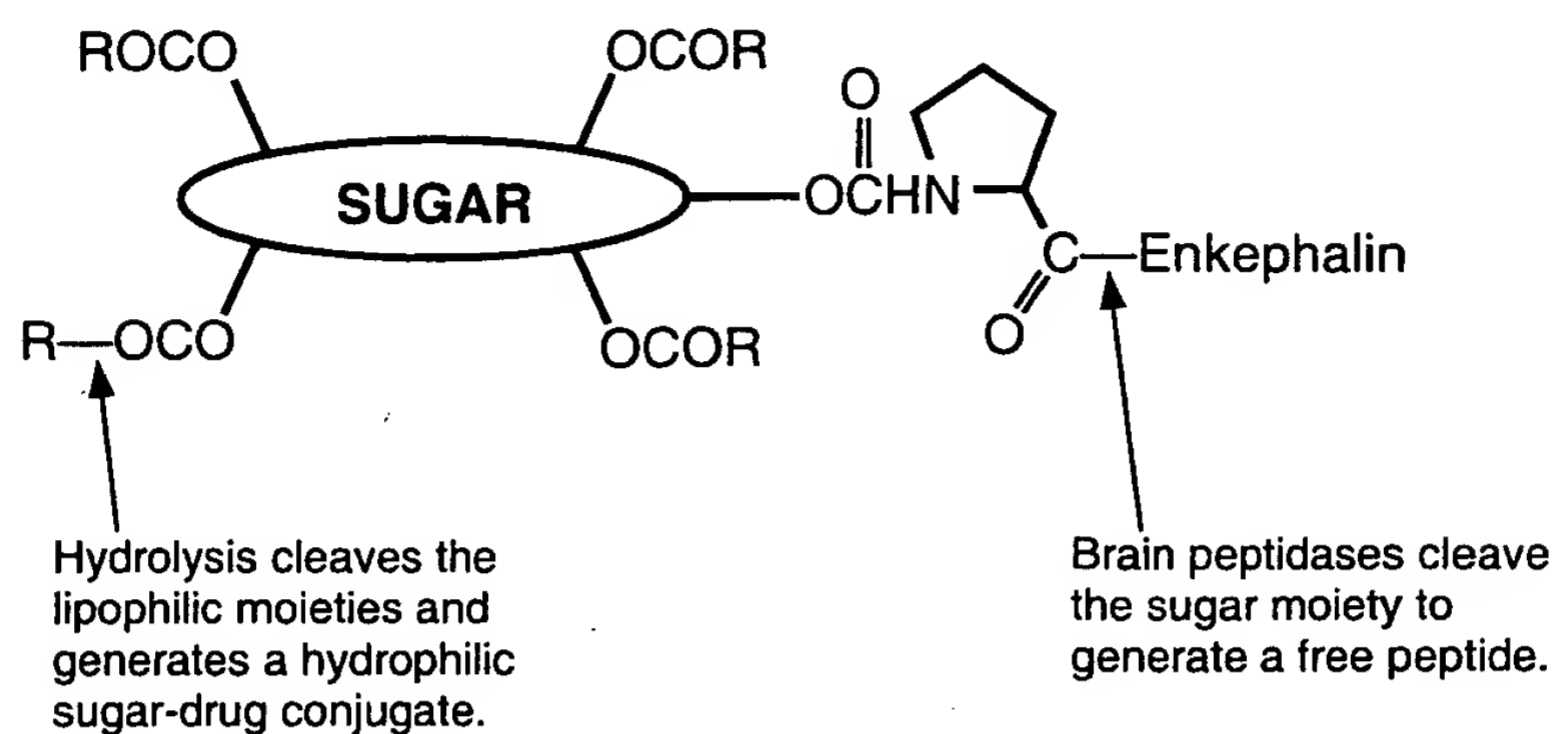


FIGURE 1A

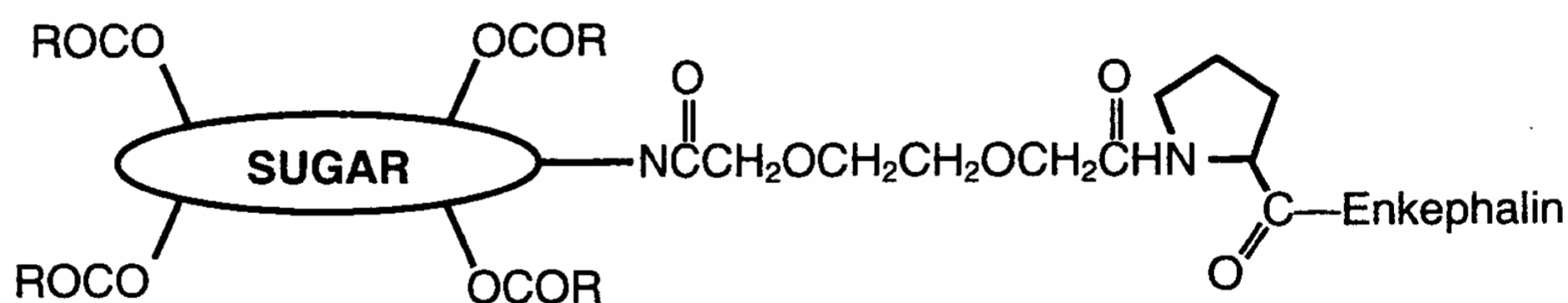


FIGURE 1B

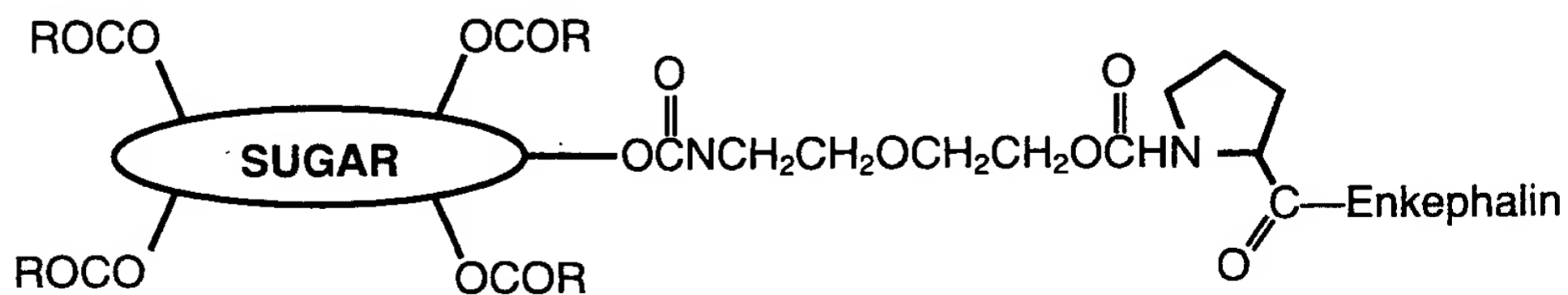
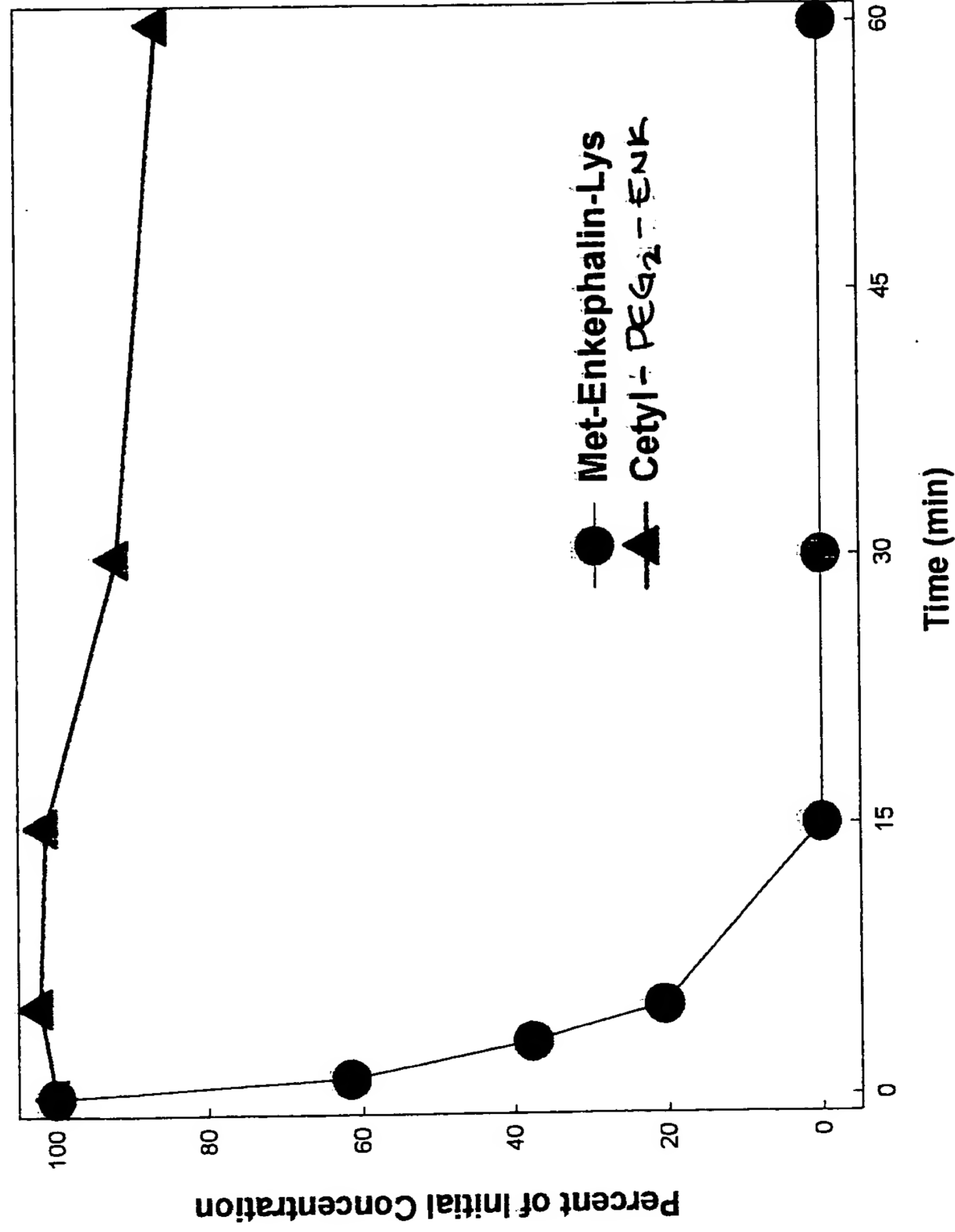


FIGURE 1C

Stability of Enkephalin and Cetyl-PEG₂-Enkephalin in Rat Brain Homogenate



2 % Rat Brain in
PBS buffer, pH 7.4, 37 C
Peptide = 60 ug/mL

FIGURE 2

Stability of Cetyl-PEG₂ Enkephalin in Rat Brain Homogenate

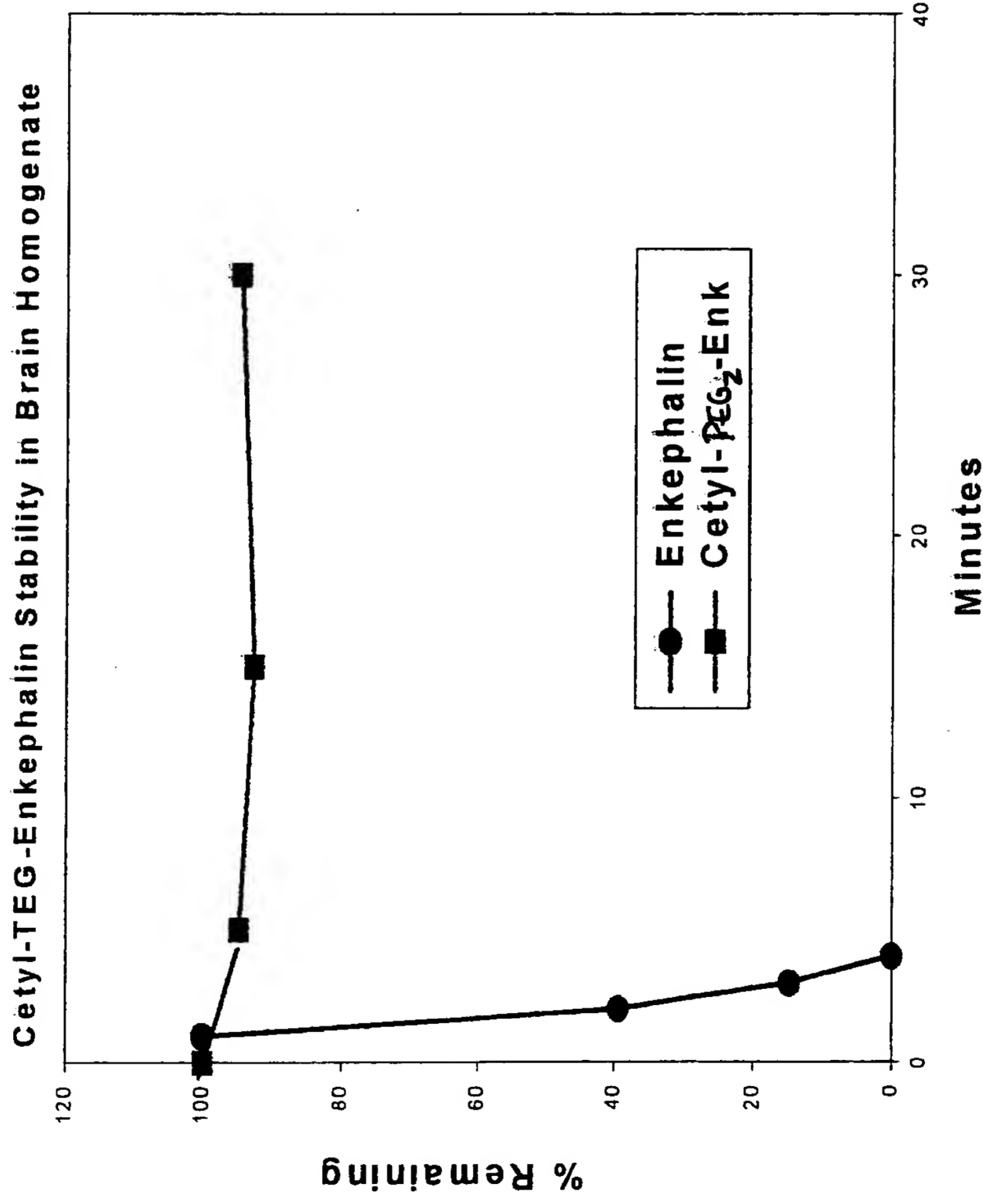


FIGURE 3

Stability of Palmitate- PEG_3 -Enkephalin in Rat Brain Homogenate

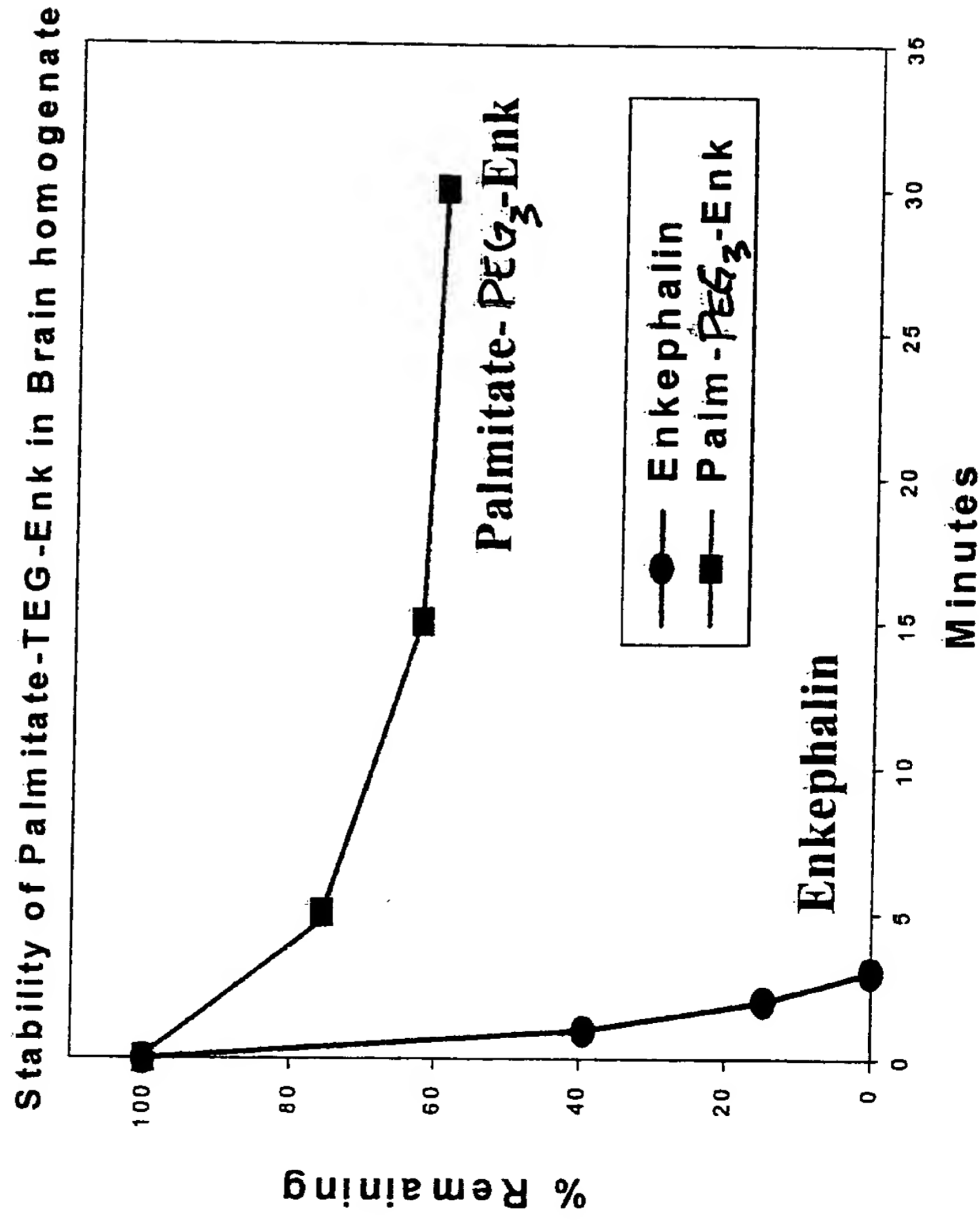


FIGURE 4

Isolation of Cetyl-PEG₂-Enkephalin from the Brain

FIGURE 5A

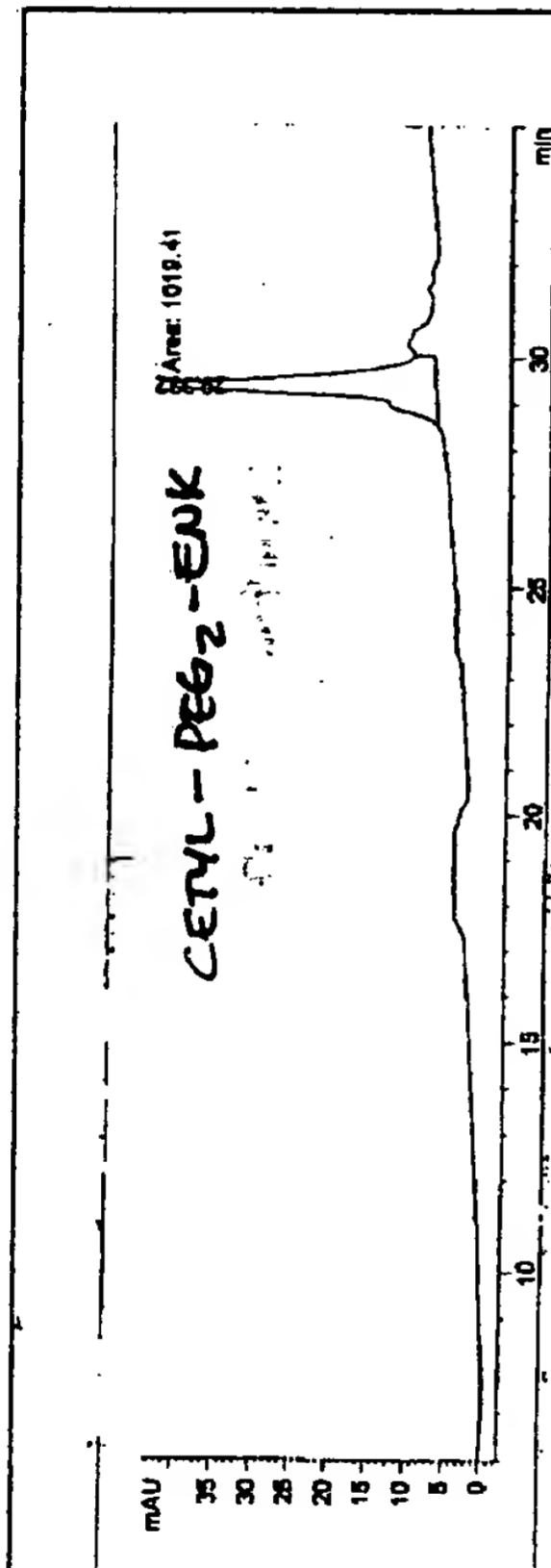


FIGURE 5B

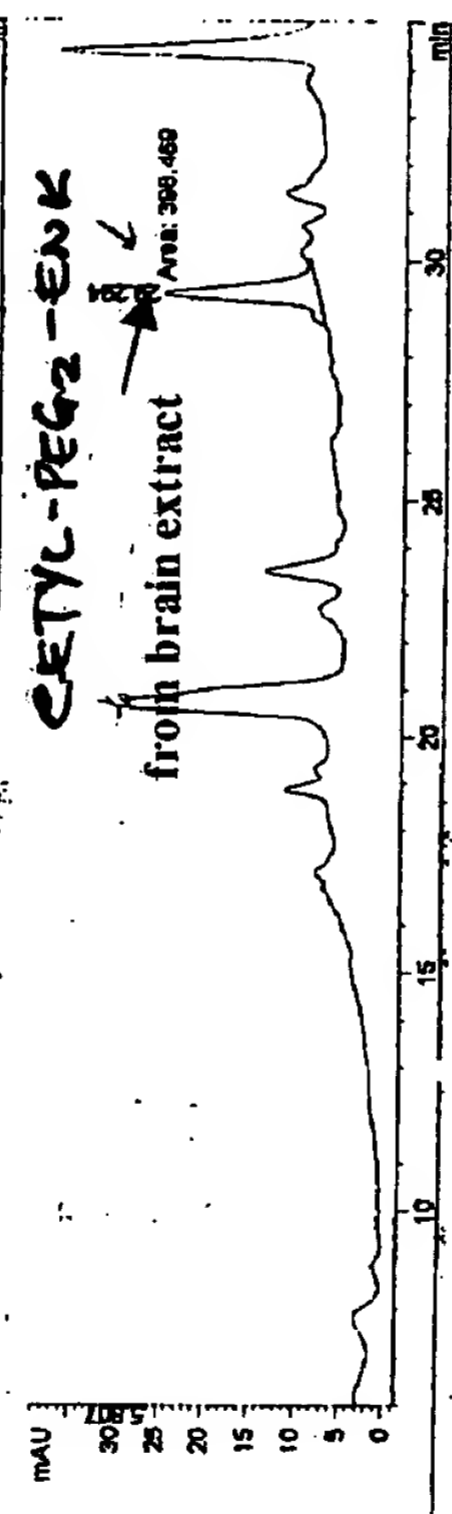


FIGURE 5C

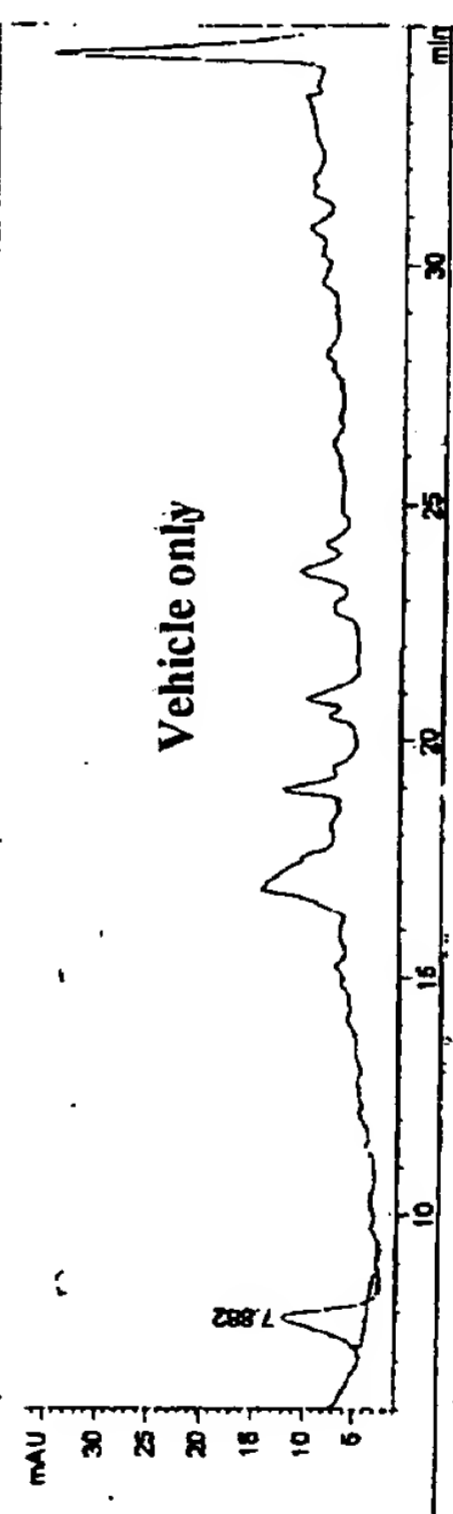
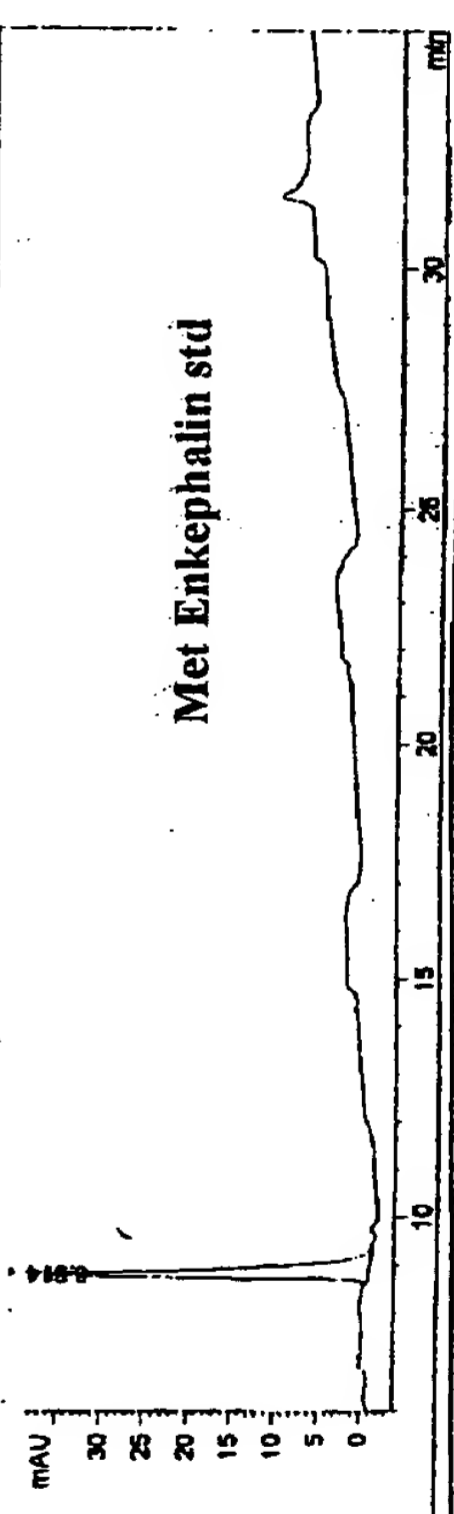


FIGURE 5D



HPLC conditions:
 Column: C-18
 Solvent: solvent A: IPA
 solvent B: Water
 +0.1% TFA
 Gradient: linear

Naloxone Antagonism of Cetyl-PEG₂-Enkephalin-Induced Analgesia

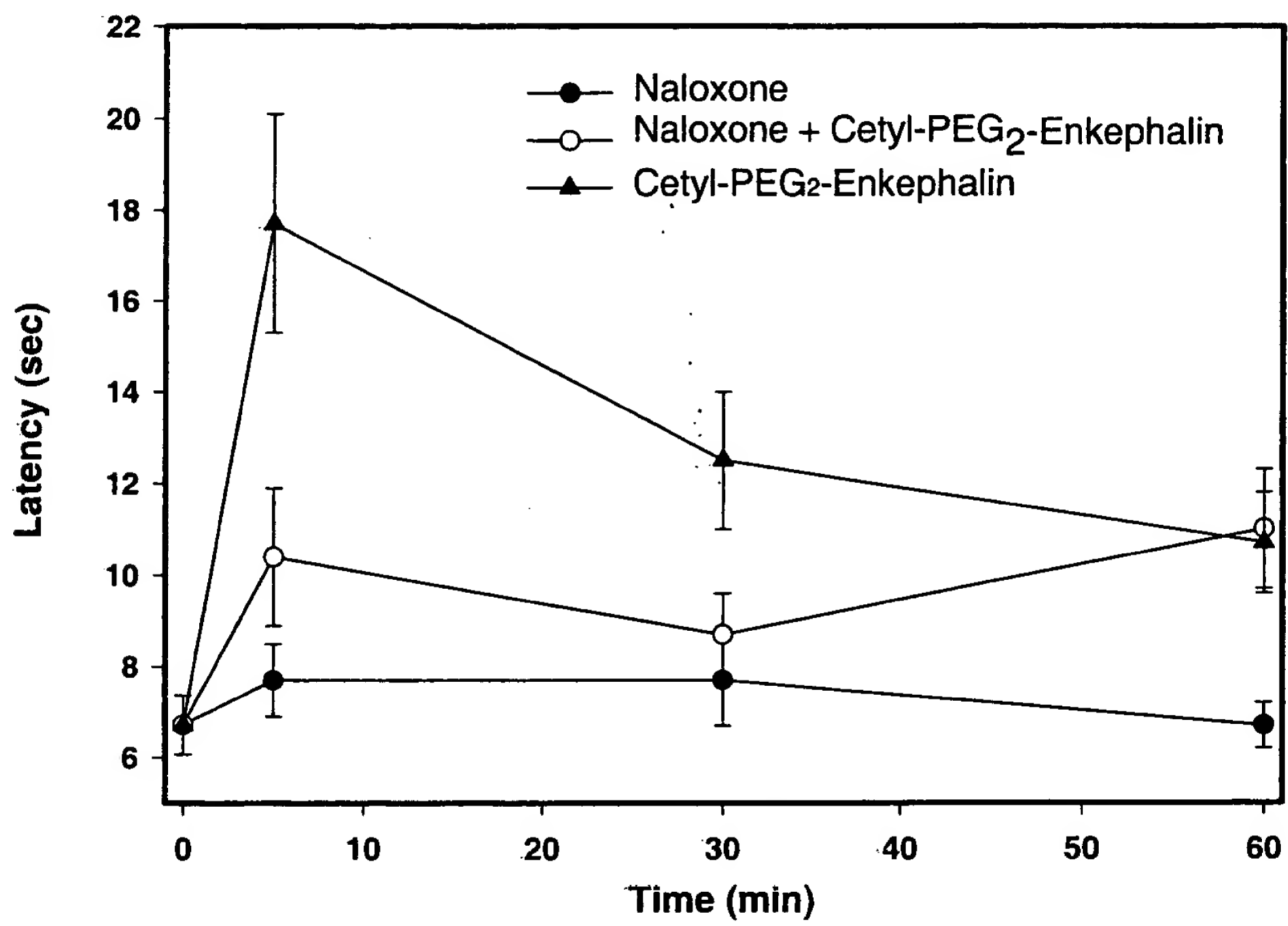


FIGURE 6

Analgesic Effect of a 5 mg/kg IV Dose of Cetyl-PEG₂-Enkephalin
Monoconjugate in the Rat Hot-Plate Assay

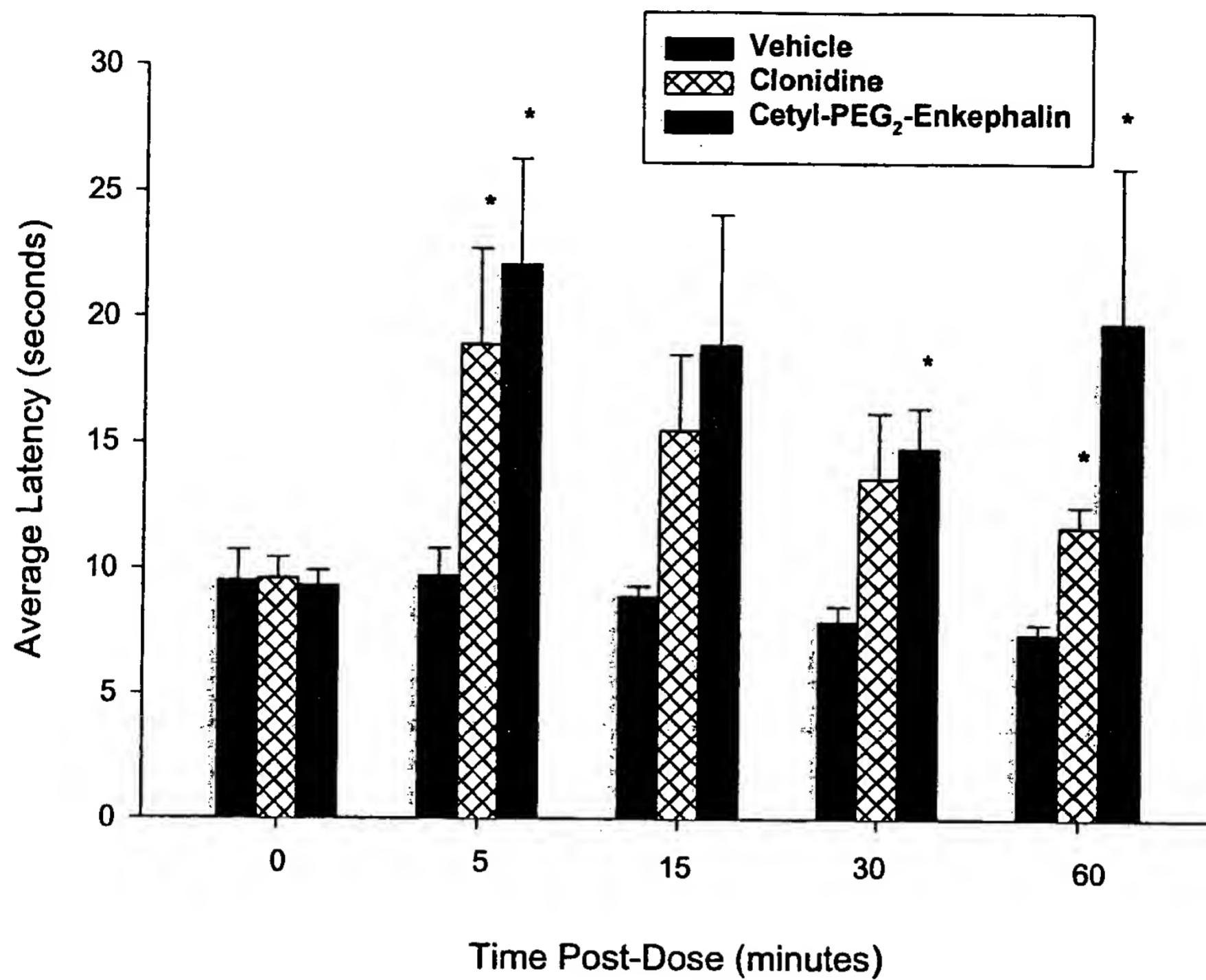


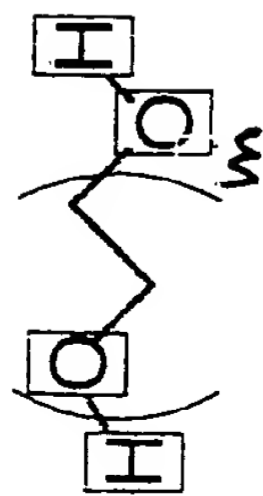
FIGURE 7

COMPARISON OF μ -RECEPTOR BINDING AFFINITY OF ENKEPHALIN CONJUGATES		
DRUG OR CONJUGATE	DETAILED STRUCTURE	% SPECIFIC BINDING*
Naloxone	Naloxone	100
Enkephalin	Met-Enkephalin	67
Cetyl-ENK	Cetyl-PEG ₂ -ENK	100
Chol-ENK	Cholesterol-PEG ₃ -ENK	95
DHA-ENK	DHA-PEG ₂ -ENK	63
Palm-ENK	Palmitate-PEG ₃ -ENK	76
Cetyl-TEG-ENK	Cetyl-PEG ₃ -ENK	100

*Data are based on percent inhibition at a concentration of 100nM. The radioligand was DAMGO ([D-Ala², N-Me-Phe-Gly⁵-ol]enkephalin) and naloxone served as the reference.

FIGURE 8

Synthesis of Oligomer



Polyethylene glycol

$m = 0, 1, 2, 3$

(average)

Base



Addition



$\text{Me}-(\text{CH}_2)_n-\text{Br}$

(Bromo alkyl derivative)

$m = 15, 17 \text{ etc.}$



Amiphilic Polymer

"Free End"



Amiphilic Polymer

FIGURE 9

Attachment of Oligomer to Enkephalin

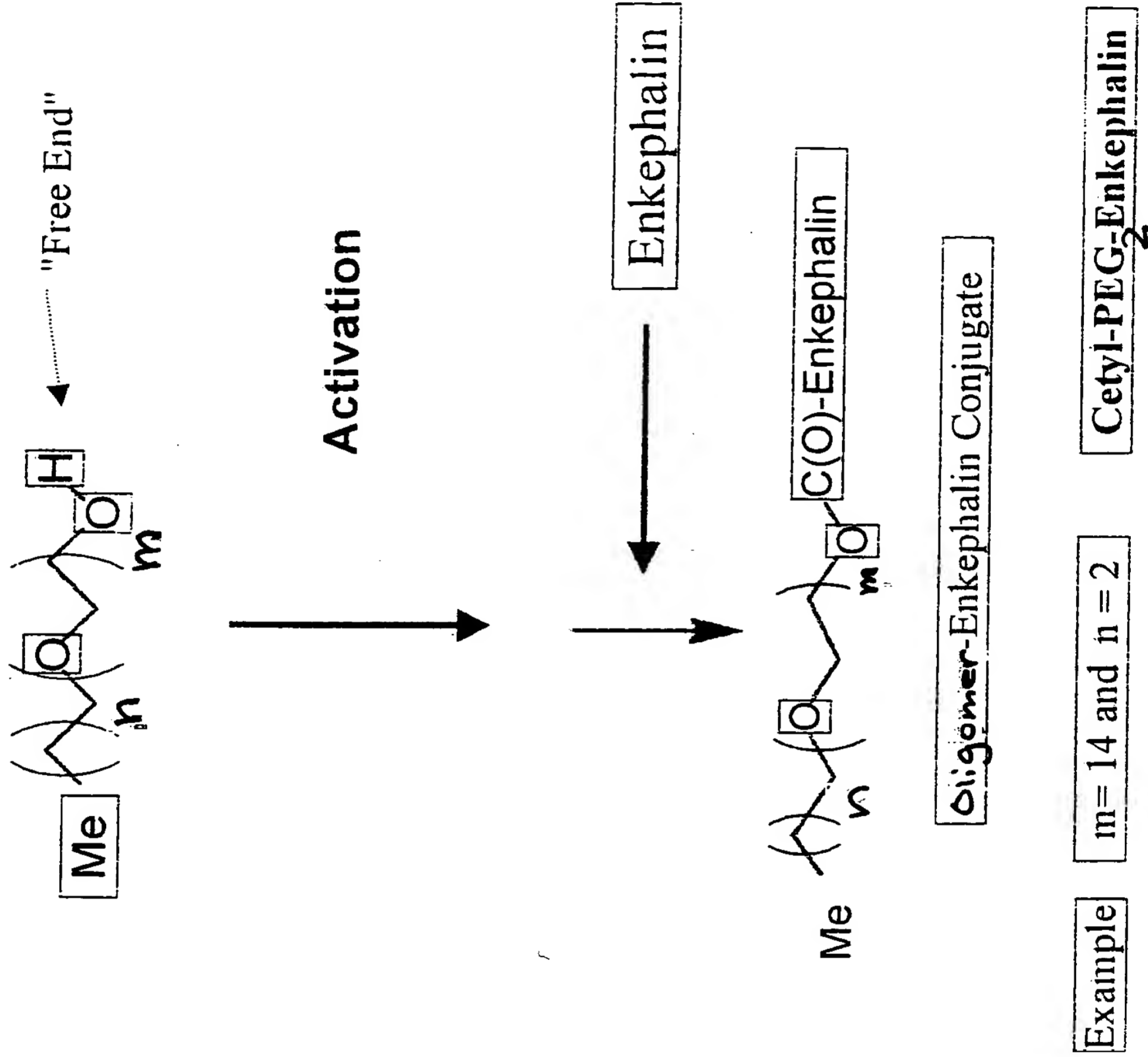


FIGURE 10